PATENT COOPERATIC.. TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 27 April 2000 (27.04.00)	
International application No. PCT/US99/22967	**Applicant's or agent's file reference** 53963PCT9A
International filing date (day/month/year) 01 October 1999 (01.10.99)	**Priority date** (day/month/year) 02 October 1998 (02.10.98)
Applicant MATSON, Charles, J. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

31 March 2000 (31.03.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Diana Nissen
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Not entered (cut-off page)

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
E 1500 PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US99/22967	01/10/1999	02/10/1998
International Patent Classification (IPC) or national classification and IPC A61K9/70		
Applicant 3M INNOVATIVE PROPERTIES COMPANY et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 12 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
31/03/2000	06.12.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Heirbaut, M Telephone No. +49 89 2399 8642

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US99/22967

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1,3-33	as originally filed			
2,2a	as received on	03/11/2000	with letter of	03/11/2000

Claims, No.:

1-11	as received on	03/11/2000	with letter of	03/11/2000

Drawings, sheets:

1/16-16/16	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☒ the claims, Nos.: 12-20
- ☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)
   see separate sheet

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 1-10.

because:

- ☒ the said international application, or the said claims Nos. 1-10 relate to the following subject matter which does not require an international preliminary examination (*specify*):
  see separate sheet
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☒ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:
see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☒ all parts.

☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	11-20
	No:	Claims	1-10
Inventive step (IS)	Yes:	Claims	
	No:	Claims	11-20
Industrial applicability (IA)	Yes:	Claims	11-20
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

I

1 The amended set of claims does not meet the requirements of Art. 34(2)(b) PCT, as it introduces subject-matter which extends beyond the content of the application as originally filed. There is no support in the application as originally filed for the feature "the ratio ... is about **1:1** to 5:1", which is only disclosed in the context of the specific embodiment of example 1, and the other features of said specific embodiment are not indicated in present claim 2.

This opinion has been established as if the above mentioned amendment had not been made, and is therefore based on the application as originally filed (Rule 70.2 (c) PCT).

III

1 Present claims 1-10 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

IV

1 The present application does not meet the requirements of unity of invention (Article 34(3) and Rule 13.1 PCT), as it does not relate to one invention only or a group of inventions so linked as to form a single general inventive concept.

The separate inventions are:

(1) A method for administering a pharmacological agent to an animal (present claims 1-7)

(2) A method for modifying a physiological system of an animal (present claims 8-10)

(3) A transmucosal drug delivery device (present claims 11-20).

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

(1) The feature "applying a transmucosal drug delivery device to a mucous membrane of the animal, wherein the device comprises an adhesive suitable for adhering the device to the mucous membrane, and a pharmacological agent" common to independent claims 1 and 8 lacks novelty (see section V, paragraph 2 of this communication)

(2) The transmucosal drug delivery device of present claims 11-20 is not required to implement the methods of present claims 1-10, as there is no reference in said method claims to said device.

V

1 Reference is made to the following documents (D):

D1: GB-A-981 372
D2: EP-A-0 654 261
D3: WO-A-9 418 925
D4: WO-A-9 630 013
D5: US-A-5 750 134 (cited in the application)
D6: US-A-5 750 136 (cited in the application)

2 The subject-matter of present independent claims 1 and 8 (method) does not meet the requirements of novelty (Article 33(2) PCT) in the light of any of the prior art documents D1-D6, which teach the combination of features indicated in said claims.

Document D1 teaches a solid formulation suitable for oral administration to animals, being in the form of wafers readily adherent to the tongue or buccal mucosa and comprising **a physiologically active substance** (eg iron or a compound thereof), a solid non-toxic adhesive, and a non-toxic humectant and plasticiser (see in particular claim 1 of D1).

Document D2 teaches a solid mucoadhesive composition for therapeutic or hygienic treatment of animals or humans, to be applied to the buccal or nasal mucosa, comprising a specific cellulose ether, a homopolymer or copolymer of acrylic acid or a physiologically acceptable salt thereof and a therapeutically or physiologically active compound (see in particular claim 1 of D2). Active compounds are eg antibiotics, antiseptics, local analgesics, anti-inflammatory compounds (see in particular page 3, lines 21-31 of D2), which are pharmacological agents effective for modifying the physiological system of an animal.

Document D3 teaches a system for mucosally administering a macromolecular drug to the oral cavity, comprising an inner drug/enhancer/ polymer layer having one surface **adapted to contact the mucosal tissue of the oral cavity and adhere thereto** when wet and an opposing surface in contact with and adhering to an overlying inert layer, said inner layer containing from about two to sixty percent by weight of a bile salt enhancer, five to sixty five percent by weight of a hydrophilic polymer and an effective amount of a macromolecular drug, having a molecular weight of at least 500 daltons (see in particular claim 1 of D3). The drug can be heparin having a molecular weight of between about 4000 and 6000 (see in particular claim 9 of D3). Heparin has potent anticoagulant properties (see in particular page 5, lines 33-35 of D3). It is stressed that heparin is a pharmacological agent effective for modifying the physiological system of

an animal.

Document D4 teaches a device which comprises a mucoadhesive matrix comprising: (1) a particulate polymeric resin with an average particle size of less than or equal to about 100 µm, and comprising at least about 55% by weight of carboxylic acid moieties based on the total weight of the polymeric resin; (2) from about 20 parts to about 250 parts by weight of a hydrophobic elastomeric component, based on 100 parts by weight of the resin; and (3) from about 0.1 to about 20 parts by weight of melatonin based on 100 parts by weight of the resin; wherein the resin is dispersed substantially throughout the elastomeric component, and which composition contains less than about 10 parts by weight of water based on the total weight of the resin (see in particular claim 1 of D4). Delivery to and across the oral mucosa is preferred (see in particular page 3, paragraph 2 of D4). It is stressed that melatonin is a pharmacological agent effective for modifying the physiological system of an animal.

Document D5 teaches a bioadhesive composition that comprises: 1) a particulate polymeric resin with an average particle size of less than or equal to about 100 µm and comprising at least about 55% by weight of carboxylic acid moieties based on the total weight of the polymeric resin; 2) from about 20 parts to about 250 parts by weight of a hydrophobic elastomeric component, based on 100 parts by weight of the resin; and 3) an amount of a drug effective to provide a desired therapeutic result wherein the resin and the drug are dispersed substantially throughout the elastomeric component, and which composition contains less than about 10% water by weight based on the weight of the polymeric resin, exhibits substantially no instantaneous adhesion to dry skin, and adheres to a mucosal surface (see in particular column 2, lines 14-32 of D5). Suitable drugs include anti-inflammatory drugs, coronary vasodilators, calcium channel blockers, bronchodilators, enzyme inhibitors, steroidal hormones, immunomodulators, antihistamines (see in particular column 7, lines 2-47 of D5), which are pharmacological agents effective for modifying the physiological system of an animal.

Document D6 teaches a bioadhesive composition that comprises: 1) a particulate polymeric resin with an average particle size of less than or equal to about 100 µm and comprising at least about 55% by weight of carboxylic acid moieties based on the total weight of the polymeric resin; 2) from about 20 parts to about 250 parts by weight of a hydrophobic elastomeric component, based on 100 parts by weight of the resin; and 3) an amount of a drug effective to provide a desired therapeutic result, wherein the resin and the drug are dispersed substantially throughout the elastomeric component, and which composition contains less than about 10% water by weight based on the weight of the polymeric resin, exhibits substantially no instantaneous adhesion to dry skin, and adheres to a mucosal surface (see in particular column 2, lines 14-32 of D6). Suitable drugs include anti-inflammatory drugs, coronary vasodilators, calcium channel blockers, bronchodilators, enzyme inhibitors, steroidal hormones, immunomodulators, antihistamines (see in particular column 7, lines 2-47 of D6), which are pharmacological agents effective for modifying the physiological system of an animal.

3 The subject-matter of present independent claim 11 (transmucosal drug delivery device) meets the requirements of novelty (Article 33(2) PCT).

None of the prior art documents cited in the international search report teaches the subject-matter having the combination of features indicated in said claim, in particular the presence of a cross-linked elastomeric polymer being 30-80% cross-linked in combination with the other indicated components.

4 The subject-matter of present independent claim 11 (drug delivery device) does not meet the requirements of inventive step (Article 33(3) PCT).

Document D4, considered to represent the closest prior art, teaches a device which comprises a mucoadhesive matrix comprising: (1) a particulate polymeric resin with an average particle size of less than or equal to about 100 µm, and comprising at least about 55% by weight of

carboxylic acid moieties based on the total weight of the polymeric resin; (2) from about 20 parts to about 250 parts by weight of a hydrophobic elastomeric component, based on 100 parts by weight of the resin; and (3) from about 0.1 to about 20 parts by weight of melatonin based on 100 parts by weight of the resin; wherein the resin is dispersed substantially throughout the elastomeric component, and which composition contains less than about 10 parts by weight of water based on the total weight of the resin (see in particular claim 1 of D4). Delivery to and across the oral mucosa is preferred (see in particular page 3, paragraph 2 of D4).

The subject-matter of present claim 11 differs from the teaching of document D4 in the presence of a cross-linked elastomeric polymer being 30-80% cross-linked in combination with the other indicated components.

The technical problem facing the skilled person at the priority date of the present application was to provide improved transmucosal drug delivery systems in terms of adhesive properties and drug release profile which can be readily altered as needed for the particular drug to be delivered (see in particular page 7, lines 16-22 of the present description).

However, it is disclosed that said improvement can only be realised with **certain ratios** of the cross-linked elastomer and polyisobutylene (see in particular page 7, lines 16-17 of the present description). As said ratios are not indicated in present claim 11, the technical problem is not solved over the whole range claimed (see also section VIII of this communication).

5 For the assessment of the present claims on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

VII

1 The present application does not meet the requirements of Rule 5.1(a)(ii) PCT, as the relevant background art disclosed in the documents D1-D4 is not mentioned in the description, nor are these documents identified therein.

VIII

1 The present application does not meet the requirements of clarity (Article 6 PCT).

1.1 It is clear from the present description that the following feature is essential to the definition of the invention:

The improvement of adhesive properties and drug release profile which can be readily altered as needed for the particular drug to be delivered, can only be realised with **certain ratios** of the cross-linked elastomer and polyisobutylene (see in particular page 7, lines 16-17 of the present description).

Since present independent claim 11 does not contain said feature, it does not meet the requirements of Article 6 PCT and Rule 6.3 (b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.

1.2 The vague and imprecise statement in the description on page 33, paragraph 2, implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them (PCT Guidelines, C-III, 4.3a).

veterinarian (or other skilled animal care provider), or prolonged hospitalization, cost prohibitive to the owner. In addition, the fractious nature of some animals can preclude safe drug administration to the animal even by skilled handlers. Moreover, in rural areas, emergency situations frequently necessitate therapeutic action sooner than a veterinarian can arrive to provide the necessary treatment. Because of these and other factors unique to providing health care to animals, physiological similarity is only one factor affecting the therapeutic benefit of a pharmacological agent across species lines.

Typically, drugs are administered to animals orally or parenterally. And, while some pharmacological agents are available in an oral dosage form, to ensure that the necessary dose is administered, many agents must be administered by injection or directly to the stomach using a stomach tube. These administration methods can ensure proper dose administration, however, repeated administration via injection or stomach tube can quickly become irritating and stressful to the animal as well as dangerous to the animal owner or health care provider.

Hence, there is a need for effective diagnostic and therapeutic products and methods for animals that are humane, cost effective, easy to administer, and safe for both the animal and the health care provider.

Summary of the Invention

The present disclosure is directed to new products and methods for safe, simple, effective, and humane treatment or diagnosis of a condition in animals. It will be appreciated, however, that many of the procedures disclosed herein can also be used advantageously for some human patients or conditions.

In several places throughout the specification, guidance is provided through lists of examples. In each instance, the recited list serves only as a representative group. It is not meant, however, that the list is exclusive.

The present invention provides safe and convenient drug delivery for short term or prolonged drug administration to a patient. The invention includes use of mucosal originated drug delivery systems. Included within mucosal originated drug delivery systems of the invention are known transmucosal drug delivery (TMDD) systems as well as new TMDD compositions. Mucosal originated drug delivery systems also include

PCT/US99/22967
3M Innovative Properties Company, et al.
Our Ref.: E 1500 PCT

CLAIMS:

1. A transmucosal drug delivery device having a composition comprising:
   - a polymeric resin;
   - a linear elastomeric polymer;
   - a cross-linked elastomeric polymer being 30-80% cross-linked; and
   - a pharmacological agent,

   wherein the ratio of linear elastomeric polymer to cross-linked elastomeric polymer is about 1:2 to 5:1.

2. The transmucosal drug delivery device according to claim 1 wherein the ratio of linear elastomeric polymer to cross-linked elastomeric polymer is about 1:~~2~~ 1 to 5:1.

3. A transmucosal drug delivery device according to claim 1 wherein:
   (i) the polymeric resin is a particulate polymeric resin present in an amount of from about 40 to about 65 percent by weight based on the total weight of the composition;
   (ii) the linear elastomeric polymer is present in an amount of from about 15

~~35~~ 1

to about 50 percent by weight based on the total weight of the composition; and

(iii) the cross-linked elastomeric polymer is present in an amount of from about 5 to about 30 percent by weight based on the total weight of the composition.

4. The transmucosal drug delivery device according to claim 3 wherein the particulate polymeric resin is a linear polyacrylic acid resin.

5. The transmucosal drug delivery device according to claim 3 wherein the linear elastomeric polymer is selected from the group consisting of polyisobutylene, polyisoprene and mixtures thereof.

6. The transmucosal drug delivery device according to claim 3 wherein the cross-linked elastomeric polymer is a cross-linked butyl terpolymer rubber.

7. The transmucosal drug delivery device according to claim 3 further comprising a penetration enhancer.

8. The transmucosal drug delivery device according to claim 1 wherein the pharmacological agent is selected from the group consisting of detomidine, medetomidine, dexmedetomidine atapamazole, fentanyl, ketamine and pharmaceutically acceptably salts thereof.

9. The transmucosal drug delivery device according to claim 7 wherein the pharmacological agent is present in an amount of from about 2 to about 5 percent by weight based on the total weight of the composition and the pharmacological agent is selected from the group consisting of medetomidine, dexmedetomidine and pharmaceutically acceptable salts thereof; and glycerol monolaurate is present in an amount of from about 0.5 to 5 percent by weight based on the total weight of

the composition.

10. The transmucosal drug delivery device according to claim 1 wherein the pharmacological agent is present in an amount from about 0.5 to about 10 percent based on the total weight of the composition.

11. A method for administering a pharmacological agent to an animal affected by a condition that is ameliorated by receiving the pharmacological agent, the method comprising:

- applying a transmucosal drug delivery device as described in claims 1 to 10 to a mucous membrane of the animal.

PCT

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(71) Applicant *(for all designated States except US)*: 3M INNOVATIVE PROPERTIES COMPANY [US/US]; 3M Center, P.O. Box 33427, Saint Paul, MN 55133–3427 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: MATSON, Charles, J. [US/US]; 13787 Greenwood Trail, Stillwater, MN 55082 (US). CHEN, Yen-Lane [US/US]; 2620 Ashley Terrace, New Brighton, MN 55112 (US). RUTH, Daniel, T. [US/US]; 9820 Justin Trail, Mahtomedi, MN 55115 (US). BENES, Luce, R., M. [FR/FR]; 18 allée du Clos Fleuri, F–45000 Orléans (FR). BURGAUD, Sophie, G. [FR/FR]; 25, rue Lionnaise, F–49100 Angers (FR). HORRIERE, Françoise, L., R. [FR/FR]; 3, route de Méréville, F–91670 Angerville (FR). SEYLER, Isabelle, M., L. [FR/FR]; 28 bis, avenue de la République, F–45300 Pithiviers (FR).

(74) Agents: HOWARD, MarySusan et al.; 3M Innovative Properties Company, Office of Intellectual Property Counsel, P.O. Box 33427, Saint Paul, MN 55133–3427 (US).

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Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: MUCOSAL ORIGINATED DRUG DELIVERY SYSTEMS AND ANIMAL APPLICATIONS

(57) Abstract

The present invention is directed to mucosal originated drug delivery systems and methods for using the drug delivery system to treat conditions in animals. Conditions amenable to treatment according to the invention are also described. The described mucosal drug delivery systems provide for drug release across a mucosal membrane as well as release away from the mucosal membrane.

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INTERNATIONAL SEARCH REPORT

Inte. .onal Application No
PCT/US 99/22967

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K9/70 A61D7/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 981 372 A (PFIZER LIMITED) the whole document ---	1-3,6,8
X	EP 0 654 261 A (VETOQUINOL S.A.) 24 May 1995 (1995-05-24) the whole document ---	1,6
X	WO 94 18925 A (THERATECH, INC.) 1 September 1994 (1994-09-01) page 8, line 1 -page 10, line 9 page 21, line 21 - line 35 ---	1,6
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 March 2000	17/03/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Benz, K

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inte .onal Application No
PCT/US 99/22967

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
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1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/22967

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 1-10 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by th applicant's protest.

[ ] No protest accompanied th payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte onal Application No
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